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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,165	06/15/2005	Alexander Mark Gibson	PZ02106	9269

36335 7590 09/29/2006

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IP DEPARTMENT
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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/539,165	GIBSON ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election **without** traverse of the election of group II and the species compound (Ia) in the reply filed on 7/3/06 is acknowledged. Group (I) is withdrawn from further consideration pursuant to 37 CFR 1.142(b) and MPEP § 821.03 as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Please amend the claims to cancel non-elected group (I) and non-elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The disclosure is inadequate in the description of the method for obtaining a diagnostic PET image using a radiopharmaceutical kit of the instant claims. It is unknown whether the use of the radiopharmaceutical kit was utilized in obtaining a diagnostic PET image.

2. Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the process of an [^{18}F]-labeled tracer, [^{18}F]-1-

amino-3-fluorocyclobutane-1-carboxyic acid ([^{18}F]-FACBC) and a radiopharmaceutical kit, does not reasonably provide enablement for the method for obtaining a diagnostic image. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to perform the invention commensurate in scope with these claims.

3. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

4. *Nature of the invention, breadth of the claims*

5. The invention is drawn to a process for the production of an [^{18}F]-labeled tracer, [^{18}F]-1-amino-3-fluorocyclobutane-1-carboxyic acid ([^{18}F]-FACBC), generation of a radiopharmaceutical kit containing the [^{18}F]-labeled tracer, [^{18}F]-1-amino-3-

fluorocyclobutane-1-carboxyic acid ([^{18}F]-FACBC) and a method of using the radiopharmaceutical kit for obtaining diagnostic PET images.

6. *State of the prior art, predictability of the art, relative skill of those in the art*

7. The use of [^{18}F]-labeled compounds, such as [^{18}F]-2-fluoro-2-deoxy-D-glucose (2-FDG) for PET imaging is known as well as [^{18}F]-L-fluorodopa and other halogen isotope compounds. The advantage of the 1-amino-cycloalkyl-1-carboxylic acids are their rapid uptake and prolonged retention in tumors thus substantially improving PET imaging for areas of the body having malignant tumors, especially brain tumors. The percent dose per gram in tissues of rats after intravenous administration include 0.11%dose/gram to 0.26%dose/gram and 1.72%dose/gram in brain tumor, etc. The administration doses, toxicity levels and imaging protocols are not explicitly disclosed (US 5,817,776).

8. The PET brain imaging of a human was conducted using 6.0 mCi [^{18}F]-1-amino-3-fluorocyclobutane-1-carboxyic acid ([^{18}F]-FACBC) and 10 mCi [^{18}F]-2-fluoro-2-deoxy-D-glucose via intravenous injection over 2 min. The images of the patient's brain are disclosed in fig 2 and 3. The uptake of radioactivity in the tumor as well as in the normal tissue of the brain was is disclosed. Although this study reveals the absorbed radiation dose in rats it does not explicitly reveal any information based on the minimum toxicity levels associated with the administration with these types of compounds (Shoup et al. J. Nuc. Med. 1999, 40, 331-338).

9. *Quantity of experimentation, amount of direction or guidance, presence of working examples*

10. The disclosure is inadequate in the description of the method for obtaining a diagnostic PET image using a radiopharmaceutical kit of the instant claims. It is unknown whether the use of the radiopharmaceutical kit was utilized in obtaining a diagnostic PET image due to the lack of working examples. Due to the insufficient information, performing the disclosed method would require undue experimentation, for example the method of administration of the agent is unknown, the required doses to provide for a diagnostic PET image and the toxicity information necessary to properly administer this type of imaging agent to a patient. The imaging agent distribution data is disclosed in the prior art but this information does not clearly covey to one ordinarily skilled in the art the correct dosage requirement necessary to obtain an improved PET image with low levels of toxicity.

Claim Rejections - 35 USC § 103

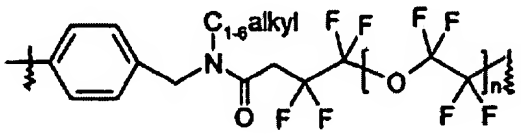
1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luthra et al. (WO 03/002157 A1) in view of Goodman (WO 97/17092).

3. Luthra et al. (WO 03/002157 A1) discloses the process for the production of an [^{18}F]-labeled tracer which comprises treatment of a resin-bound precursor (Ia) with ^{18}F. The process may also include removal of excess ^{18}F by ion-exchange chromatography,

removal of any protecting groups, removal of organic solvent and formulation of the resultant compound as an aqueous solution (p2, lines 29+; p3, lines 1-11). The linker may include the polyfluorinated compound below (p 5):



4. The inclusion of the resin-bound precursor is provided as part of a kit for PET. The kit may include a cartridge that may further include a column to remove unwanted fluoride ion and an appropriate vessel connected to allow the solvent to be evaporated. The kit is a vessel containing resin-bound precursor, a means for eluting the vessel with ^{18}F and ion-exchange cartridge and a means for deprotection of any protecting groups (p17; claim 13). Luthra et al. (WO 03/002157 A1) does not disclose the production of the compound [^{18}F]-1-amino-3-fluorocyclobutane-1-carboxyic acid ([^{18}F]-FACBC) via this solid-support method.

5. Goodman (WO 97/17092) discloses the compound [^{18}F]-1-amino-3-fluroocyclobutane-1-carboxyic acid ([^{18}F]-FACBC), the pharmaceutical composition and its use as an *in vivo* imaging agent for use in PET (p5-6). The [^{18}F] fluorination of a 1-t-butylcarbamate-3-trifluoromethane sulfonoxycyclobutane-1-carboxylic acid methyl ester occurs in a sealed vessel where [^{18}F]-fluoride was added to the vessel containing a cryptand Kryptofix, the excess [^{18}F]-fluoride was removed from the vessel upon dilution with methylene chloride and passage through a silica gel Seppak. Deprotection was subsequently followed by the preparation of an [^{18}F]-FACBC aqueous solution and elution of this solution through an ion-retardation resin (p16, lines 25+).

6. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize the solid-support method of preparing compounds, such as that of Luthra et al. (WO 03/002157 A1) due to the ease of synthesis whereby excess reagents may be simply washed away from the resin bound molecules of interest and ease of purification due to the ability to cleave the desired product from the resin support at a predetermined site before or after deprotection of any protecting groups. The linker of Luthra et al. (WO 03/002157 A1) is identical to that of the instant claims and is bound to a mannosepyranose or 2-deoxy-G-glucose tracers via the oxygen of the hydroxyl group prior to nucleophilic attack of $^{18}F^-$ (p25, example 1; claim 3). The attachment of the linker to the 1-BOCamino-3-hydroxycyclobutane-1-carboxyic acid methyl ester precursor is also via the oxygen of the hydroxyl group in the instant claims. It would have been obvious to use the 1-BOCamino-3-hydroxycyclobutane-1-carboxyic acid methyl ester precursor (p13, 10) of Goodman (WO 97/17092) and attach it to the solid-support resin linker system of Luthra et al. (WO 03/002157 A1) via the oxygen of the hydroxyl group to enact the same nucleophilic substitution of $^{18}F^-$ to generate the [^{18}F]-1-amino-3-fluroocyclobutane-1-carboxyic acid ([^{18}F]-FACBC) of Goodman (WO 97/17092) with relative ease.

Conclusion

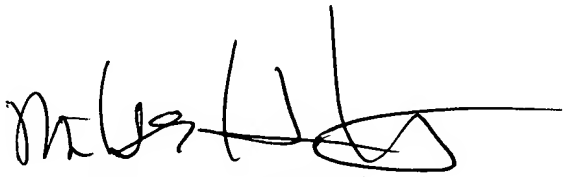
No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
August 23, 2006



MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER